Celldex therapeutics

Targeted Antibody Therapeutics to Address Devastating Diseases

AAAAI Investor & Analyst Event

NASDAQ: CLDX
February 25, 2024

Safe Harbor Statement

This communication contains "forward-looking" statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical fact are statements that could be forward-looking statements. You can identify these forward-looking statements through our use of words such as “may,” “will,” “can,” “anticipate,” “assume,” “should,” “indicate,” “would,” “believe,” “contemplate,” “expect,” “seek,” “estimate,” “continue,” “plan,” “point to,” “project,” “predict,” “could,” “intend,” “target,” “potential” and other similar words and expressions of the future. These forward-looking statements are subject to risks and uncertainties that may cause actual future experience and results to differ materially from those discussed in these forward-looking statements. Important factors that might cause such a difference include, but are not limited to, the timing, cost and uncertainty of obtaining regulatory approvals for product candidates; our ability to develop and commercialize products before competitors that are superior to the alternatives developed by such competitors; the validity of our patents and our ability to avoid intellectual property litigation, which can be costly and divert management time and attention; and the other factors listed under “Risk Factors” in our filings with the SEC, including Forms 10-K, 10-Q and 8-K. Celldex does not undertake any obligation to release publicly any revisions to such forward-looking statement to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events.

Marcus Maurer, MD

Professor of Dermatology and Allergy, Co-Director for the Fraunhofer Site for Allergology and Immunology of the Fraunhofer Translational Medicine and Pharmacology ITMP and Executive Director for the Institute of Allergology, Charité - Universitätsmedizin Berlin, Germany.

Prof Maurer is a Dermatologist and Allergologist, and he also trained in experimental pathology at the Beth Israel Deaconess Hospital and Harvard Medical School in Boston (1995-1998); Board certification for Dermatology (2000) and Allergology (2003). Assistant Professor at the Allergie-Centrum-Charité at Charité – Universitätsmedizin Berlin (2004-2005). Since 2005, full professor at Charité. Prof. Maurer a coordinator of the Global Allergy and Asthma European Networks of urticaria and angioedema centers of reference and excellence, UCARE and ACARE. His areas of clinical interest include angioedema, urticaria, mastocytosis, pruritus, skin infections, and allergic diseases. His research is focused on the biology of mast cells, neuroimmunology, inflammation, innate immunity and tolerance. He has supervised more than 60 clinical trials, phase 1 through 4. Prof. Maurer has contributed to more than 670 publications in peer-reviewed journals (>32.000 citations, H Index 91) and 51 books and book chapters.

Allen Kaplan, MD

Professor of Medicine, Division of Pulmonary, Critical Care, Allergy and Immunology at the Medical University of South Carolina

Dr. Allen Kaplan graduated from Downstate Medical School (SUNY-Brooklyn) and completed his Residency in Medicine at Strong Memorial Hospital in Rochester, NY. From there he spent two years as a Clinical Fellow in the Arthritis and Rheumatism Branch of The National Institute of Arthritis and Metabolic Diseases followed by a Fellowship in Allergy and Clinical Immunology at the Harvard Medical School - Robert B. Brigham Hospital. He then returned to NIH as Head of the Allergic Diseases Section of NIAID where he remained for six years (1972-1978) and established the Allergic Diseases Center at NIH. Dr. Kaplan next moved to Stony Brook University where he was Head of the Division of Allergy, Rheumatology, and Clinical Immunology for 9 years, and was then named Chairman of the Department of Medicine. He remained at Stony Brook for 19 years and then came to The Medical University of South Carolina as Professor of Medicine. He is board certified in Internal Medicine, Allergy and Clinical Immunology, Rheumatology and Diagnostic Laboratory Immunology.

Dr. Kaplan was President of AAAAI in 1989, President of the Clinical Immunology Society in 1990, and President of The World Allergy Organization (WAO/IAACI) from 2000-2003. Author of over 380 publications, his major areas of interest are the mechanisms for production of bradykinin and its role in human disease, as well as the pathogenesis and treatment of urticaria and angioedema. He edited The Journal of The World Allergy Organization for five years, edited the textbook “Allergy”, was Co-Editor, with Dr. Malcolm Greaves, of a text entitled, Urticaria and Angioedema”, and is Co-Editor of the two-volume textbook “Allergy and Allergic Diseases”.

Celldex Team Members/Speakers

Anthony Marucci, Founder, President and Chief Executive Officer

Tibor Keler, PhD, Founder, Executive Vice President and Chief Scientific Officer

Diane Young, MD, Senior Vice President and Chief Medical Officer

Margo Heath-Chiozzi, MD, Senior Vice President, Regulatory Affairs

Diego Alvarado, PhD, Executive Director, Research

Sarah Cavanaugh, Senior Vice President, Corporate Affairs

An Exciting Year Ahead for Barzolvolimab

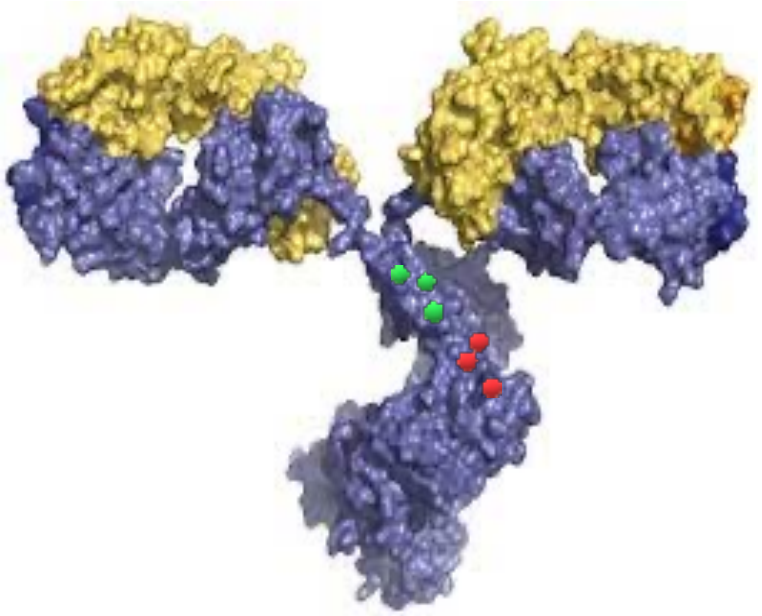
Barzolvolimab (CDX-0159)

- February 2024 – Phase 2 CSU 12-week data (late breaking oral AAAAI)
- Early 2024 – Phase 2 PN initiation
- Summer 2024 – Phase 3 CSU initiation
- 2H 2024 – Phase 2 CIndU data
- 2H 2024 – Phase 2 CSU 52-week data
- 2H 2024 – New indication identified

Barzolvolimab: Best in Class KIT Antagonist mAb

- Sub-nanomolar affinity for KIT dimerization domain
- Unique allosteric mechanism of KIT inhibition by preventing KIT receptor dimerization
- Proven MoA with rapid and profound decrease in tryptase and depletion of skin mast cells
- Product profile optimized through engineering of Fc domain
  - Eliminated all measurable FcgR and C1q binding to minimize mast cell activation
  - Added YTE mutation to provide extended half-life and support less frequent administration
- Robust manufacturing process with stable high concentration formulation
- Completed four toxicology studies to support BLA filing

Barzolvolimab



IgG1k with modified Fc

Completed Toxicology Studies to Support BLA

3 NHP Studies with multiple doses up to 75 mg/kg Q2W for 6 months

- Well tolerated with expected findings related to systemic KIT suppression:
  - Transient decreases in red blood cell mass parameters
  - Diffuse and recoverable fur lightening
  - Profound and fully recoverable reduction of sperm concentration
- No histological changes in female reproductive tissues observed
- Data peer reviewed by experts

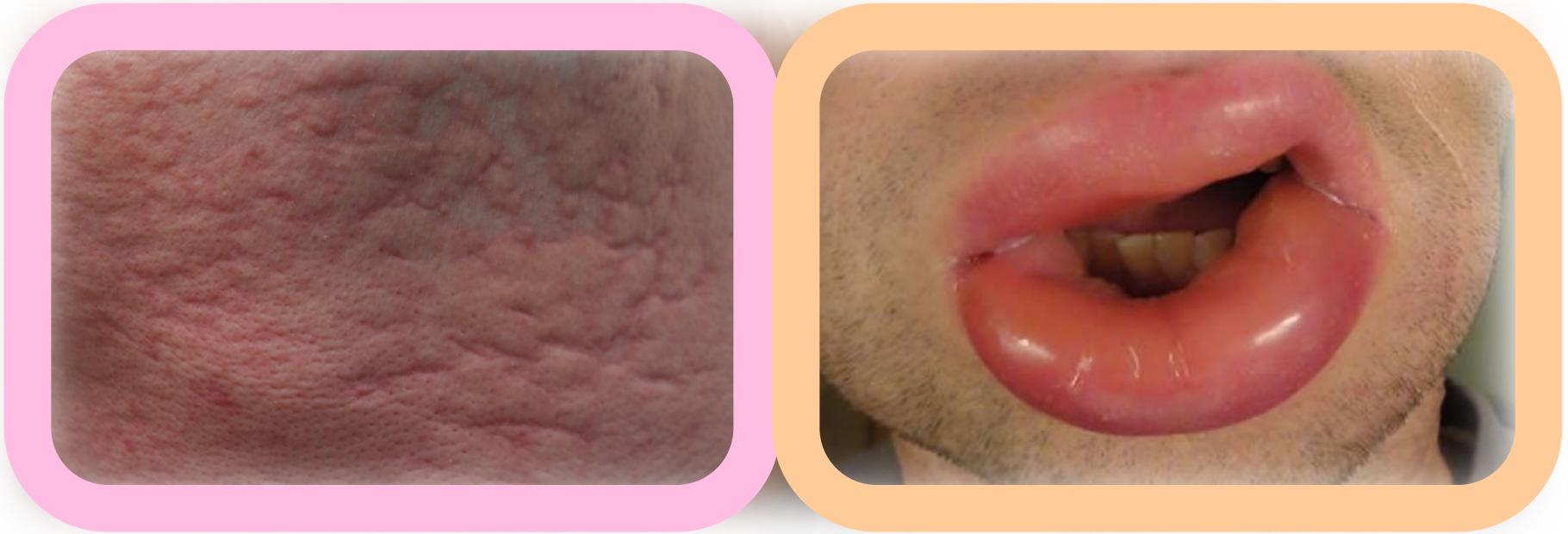
NHP study on maternal and fetal/infant development

- Mothers dosed throughout pregnancy at 75 mg/kg Q2W
  - Normal pregnancies with no clinically adverse effects noted on mothers
  - Diffuse fur lightening noted
- Infants born healthy with no development or growth issues observed through 6 months of age
  - Infants born with varying amounts of white fur and lightened skin
  - No adverse findings noted in reproductive tissues of male or female infants

Celldex therapeutics

Chronic Spontaneous Urticaria

Urticaria



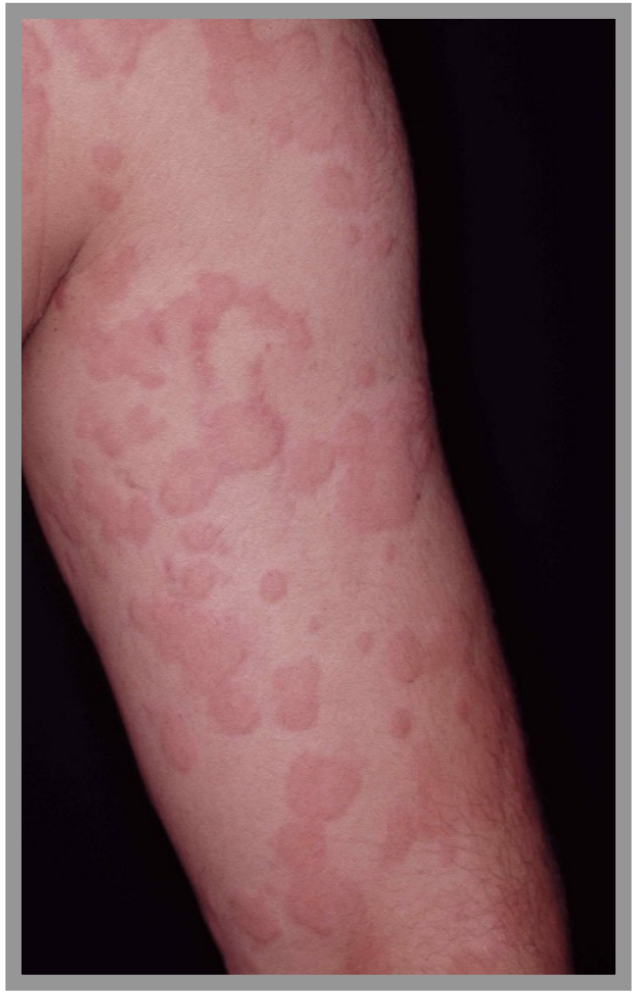
Itchy Wheals and/or Angioedema

Maurer et al., *Allergy* 2011; 66: 317-30

Chronic Urticaria = longer than 6 weeks

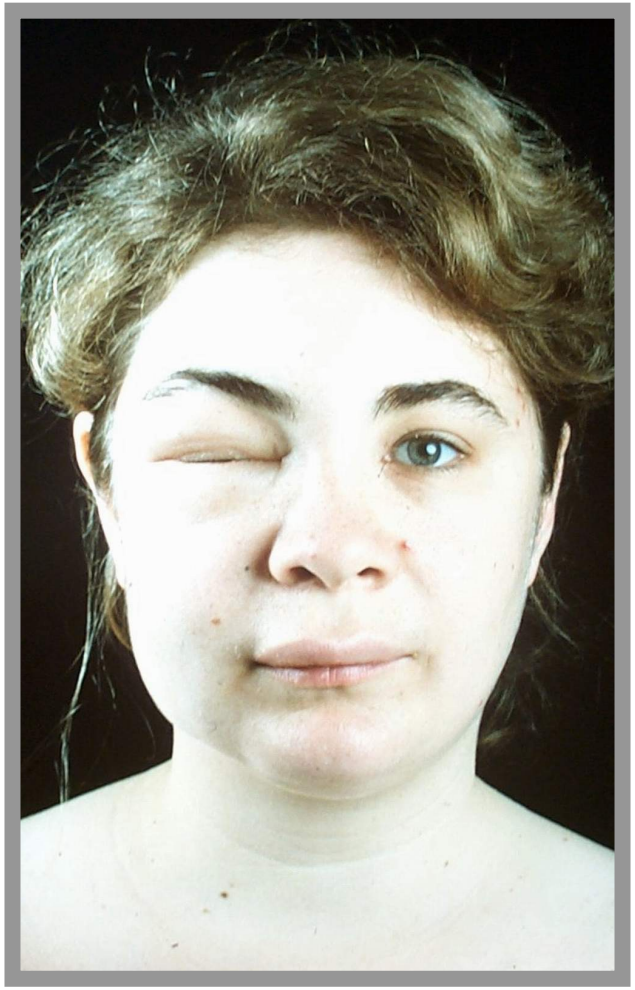
Spontaneous Urticaria (CSU)	Inducible Urticaria (CindU)
Due to known cause	Physical urticaria Symptomatic dermographism Cold Urticaria Delayed pressure urticaria Solar urticaria Heat urticaria Vibratory angioedema Cholinergic urticaria Contact urticaria Aquagenic urticaria
Due to unknown cause	

Maurer et al., *Handb. Exp. Pharmacol.* 2022; 268: 117-133



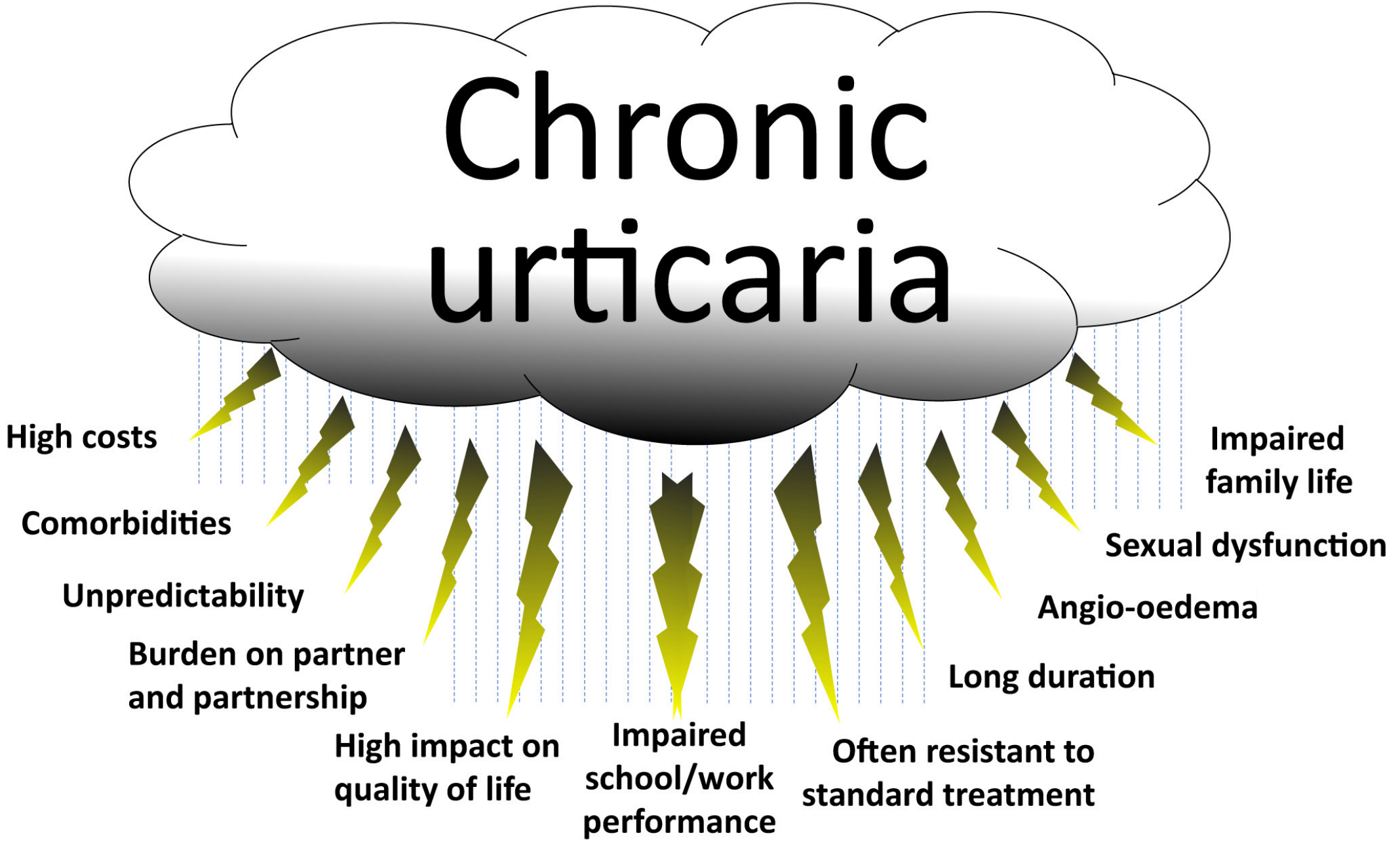
Severe pruritus

Several hours



Burning, painful

Several days

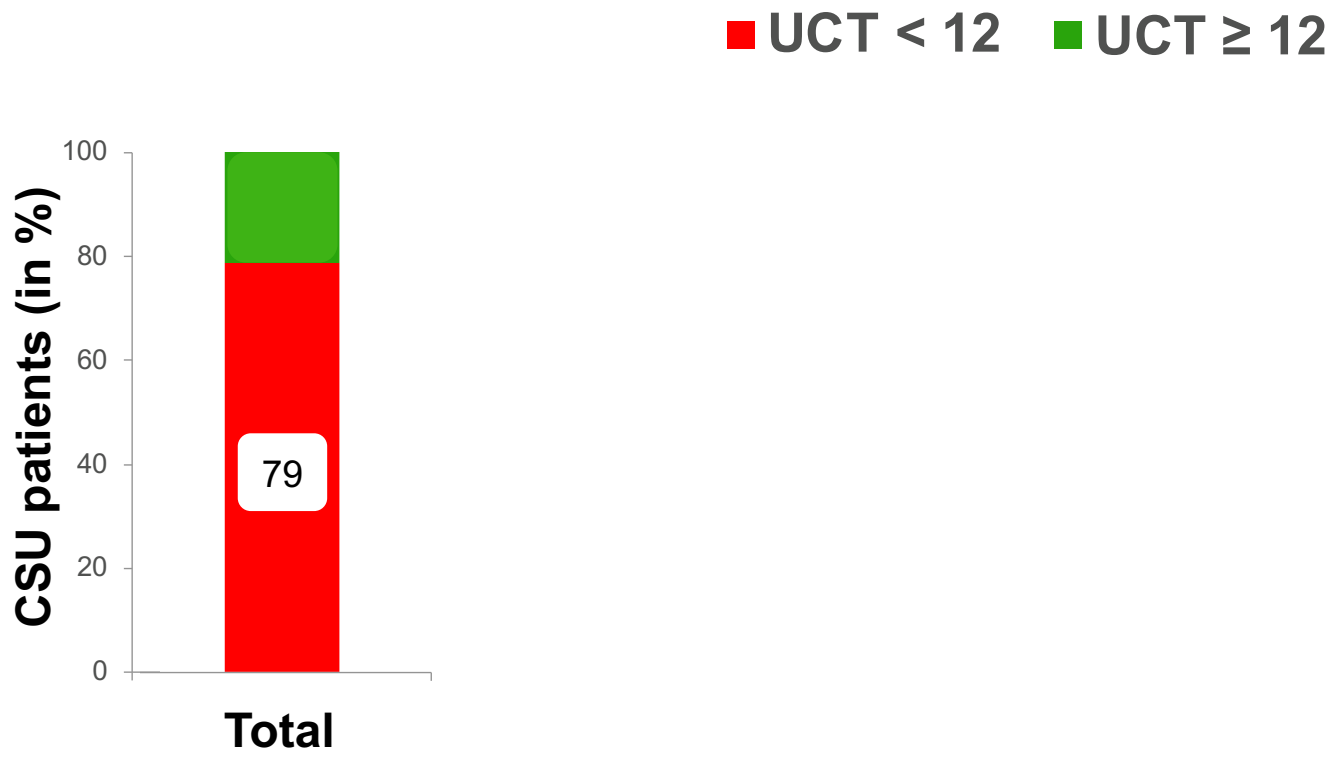


Gonçalo et al., *Br. J. Dermatol.* 2021; 184: 226-236

Chronic Spontaneous Urticaria is Chronic…

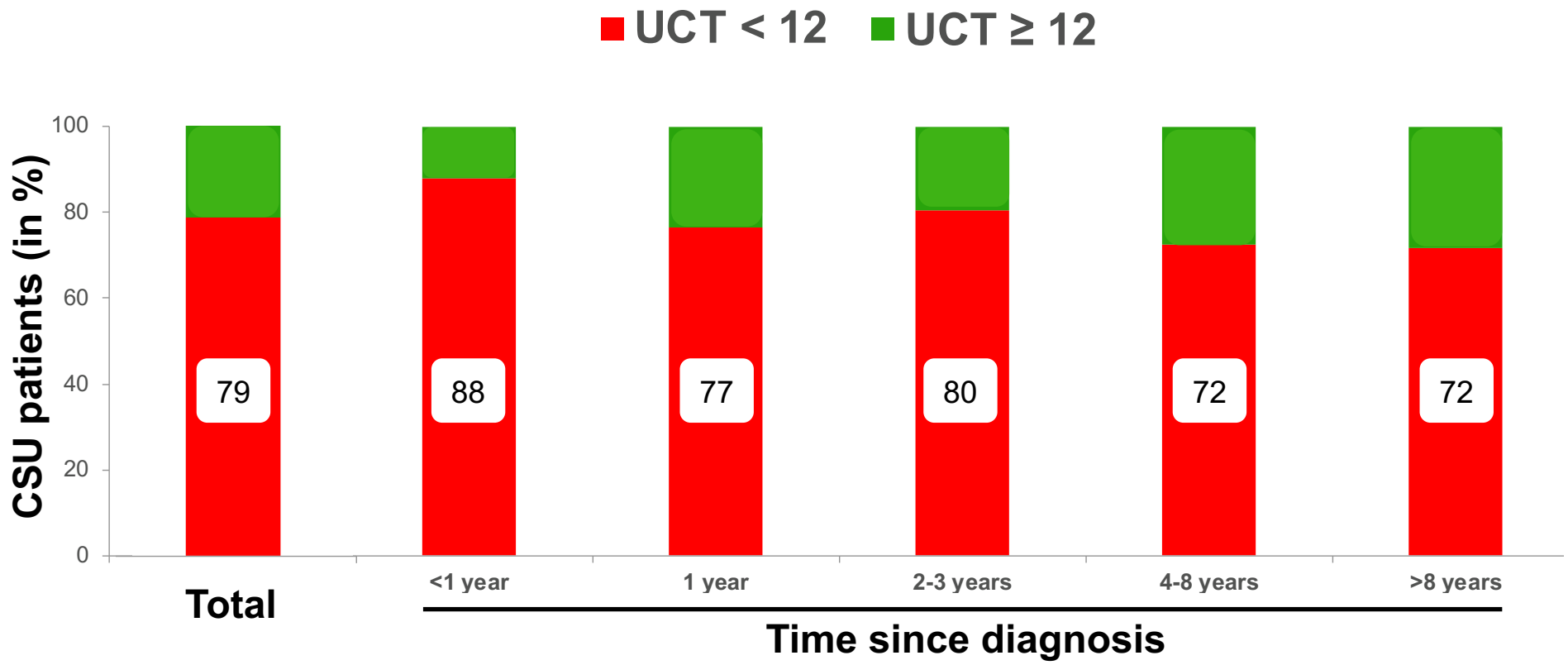
5-7 years on average

Only one in five patients with chronic urticaria has her/his disease under control



Maurer et al., *Clin. Exp. Allergy* 2017: 47; 684-692

Only one in five patients with chronic urticaria has her/his disease under control



Maurer et al., *Clin. Exp. Allergy* 2017: 47; 684-692

Chronic urticaria is a heterogenous, common, disabling, chronic disease that is often poorly controlled.

What is the goal of treating patients with chronic spontaneous urticaria?

Treat the disease until it is gone!

Zuberbier et al., *Allergy* 2022; International Urticaria Guideline

Barzolvolimab Significantly Decreases Chronic Spontaneous Urticaria Disease Activity and is Well Tolerated: Top Line Results from a Phase 2 Trial

M. Maurer[1,2], I. Kobielusz-Gembala[3], E. Mitha[4], J. Leflein[5], M. Gotua[6], B. Kwiek[7], M. Metz[1,2], M. Yellin[8], C. Taglienti[8], R. Ma[8], D. Alvarado[8], E. Paradise[8], J. A. Bernstein[9]

[1]Institute of Allergology, Charité-Universitätsmedizin Berlin, corporate member of Freie Universitäts Berlin and Humboldt-Universitäts zu Berlin, Berlin, Germany [2] Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Immunology and Allergology, Berlin, Germany [3]Medicome Sp. z.o.o., Oświęcim, Poland [4]Newtown Clinical Research, Johannesburg, South Africa [5]Respiratory Medicine Research Institute of Michigan, Ypsilanti, MI, USA [6]Center of Allergy and Immunology, Tbilisi, Georgia [7]Klinika Ambroziak Dermatologia, Lazarski University; Warsaw, Poland [8]Celldex Therapeutics, Hampton, NJ, USA; [9]University of Cincinnati College of Medicine and Bernstein Allergy Group/Clinical Research Center, Cincinnati, OH, USA.

Study Identifier: (NCT05368285)

Conflict Of Interest Statement

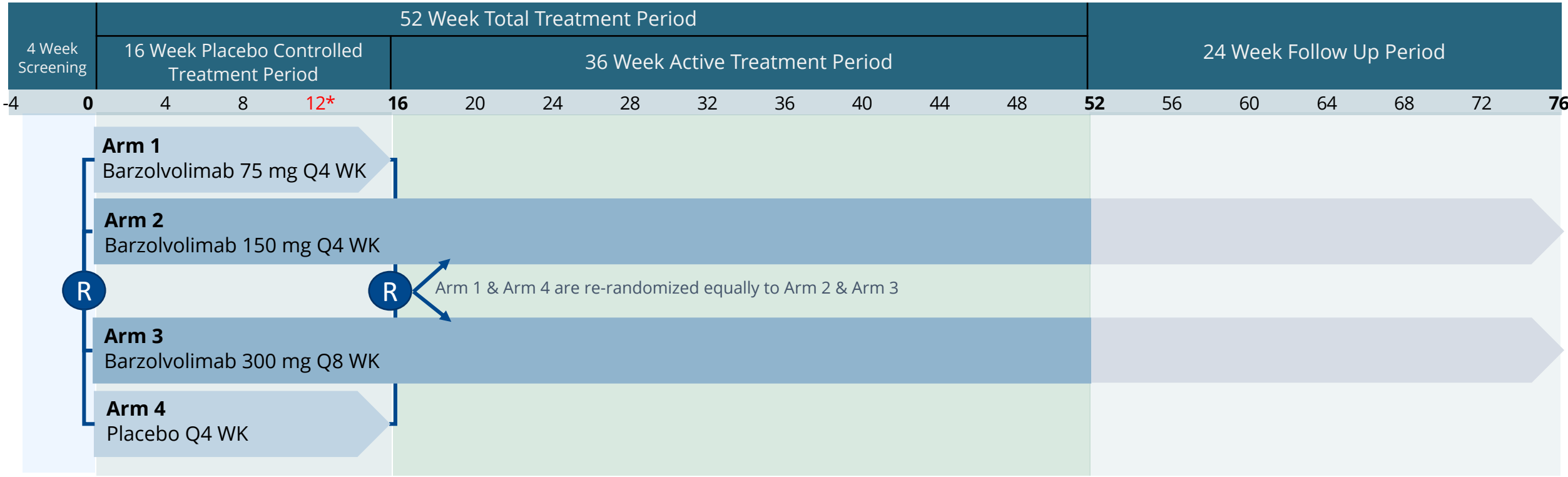
Marcus Maurer is or recently was a speaker and/or advisor for and/or has received research funding from Allakos, Alvotech, Amgen, Aquestive, Aralez, AstraZeneca, Bayer, Celldex, Celltrion, Evommune, GSK, Ipsen, Kashiv, Kyowa Kirin, Leo Pharma, Lilly, Menarini, Mitsubishi Tanabe Pharma, Moxie, Noucor, Novartis, Orion Biotechnology, Resoncance Medicine, Sanofi/Regeneron, Septerna, Trial Form Support International AB, Third HarmonicBio, ValenzaBio, Yuhan Corporation, Zurabio

Background

- Chronic spontaneous urticaria (CSU) is a mast cell driven disease characterized by itchy wheals, angioedema, or both
- Mast cells require engagement of their KIT receptors by stem cell factor (SCF) for activation, tissue recruitment and survival
- Barzolvolimab (CDX-0159), a first-in-class anti-KIT monoclonal antibody, has demonstrated improvement in itch and urticarial lesions accompanied by depletion of skin mast cells in chronic urticarias
- Here we report the primary analysis (Week 12) of a Phase 2 study evaluating the efficacy and safety of barzolvolimab compared with placebo in CSU patients whose disease is inadequately controlled by antihistamines

Study Design

A randomized, double-blind, placebo-controlled, dose-finding Phase 2 study



- Patients maintained a stable dose of a second generation H1 antihistamine at 1-4 times the approved dose throughout the study
- Rescue therapy: increase H1antihistamine dose or short course of corticosteroids

*__Primary analysis at Week 12__ (all patients who completed Week 12 or discontinued prior to Week 12)

Patient Eligibility

Key Inclusion Criteria

- Age ≥18 years
- Diagnosis of CSU ≥ 6 months
- Itch and hives for ≥ 6 consecutive weeks despite the use of 2nd generation antihistamine
- Biologic naïve/experienced patients
- Refractory to a stable 2nd generation antihistamine regimen at 1 to 4 times the approved dose
- Baseline UAS7 ≥16
- Baseline ISS7 ≥8

Key Exclusion Criteria

- Other skin conditions with symptoms of hives or angioedema
- Skin conditions associated with chronic itching that could confound the trial results
- Chronic urticaria with a clearly defined predominant or sole trigger

CSU, Chronic Spontaneous Urticaria; UAS7, weekly Urticaria Activity Score; ISS7, weekly Itch Severity Score

Study Outcomes

- Primary endpoint
  - Mean change from baseline to Week 12 in UAS7

    The UAS7 is the composite of the weekly itch severity score (ISS7) and hives severity score (HSS7) and is a widely accepted tool to measure the signs and symptoms of CSU with a score range of 0-42 (higher score indicates higher disease activity)

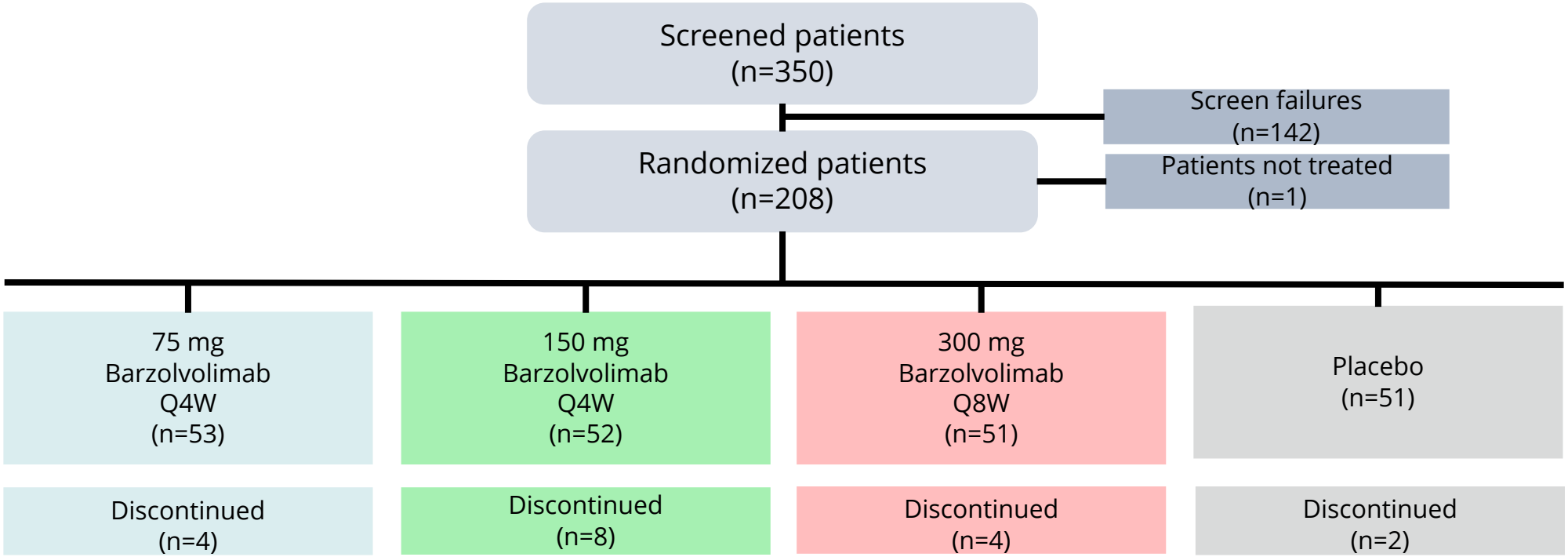
- Secondary endpoints
  - Mean change from baseline to Week 12 in ISS7
  - Mean change from baseline to Week 12 in HSS7
  - Safety and tolerability of barzolvolimab

- Exploratory analyses
  - Percentage of patients achieving UAS7≤6, UAS7=0 by Week 12
  - UAS7 response in omalizumab experienced and refractory patients

UAS7, weekly Urticaria Activity Score; ISS7, weekly Itch Severity Score; HSS7, weekly Hives Severity Score

Disposition

- In total, 350 patients screened, 208 patients randomized, 207 included in the mITT* and safety set**
- Overall, 189 (91%) completed the 12-week treatment period



*mITT population is all randomized patients who received at least 1 dose of study treatment and analyzed based on the treatment group to which they were randomized
**Safety population is all patients who received at least 1 dose of study treatment

Demographics and Baseline Characteristics

Well balanced across groups; majority of patients had severe CSU (UAS7≥28)

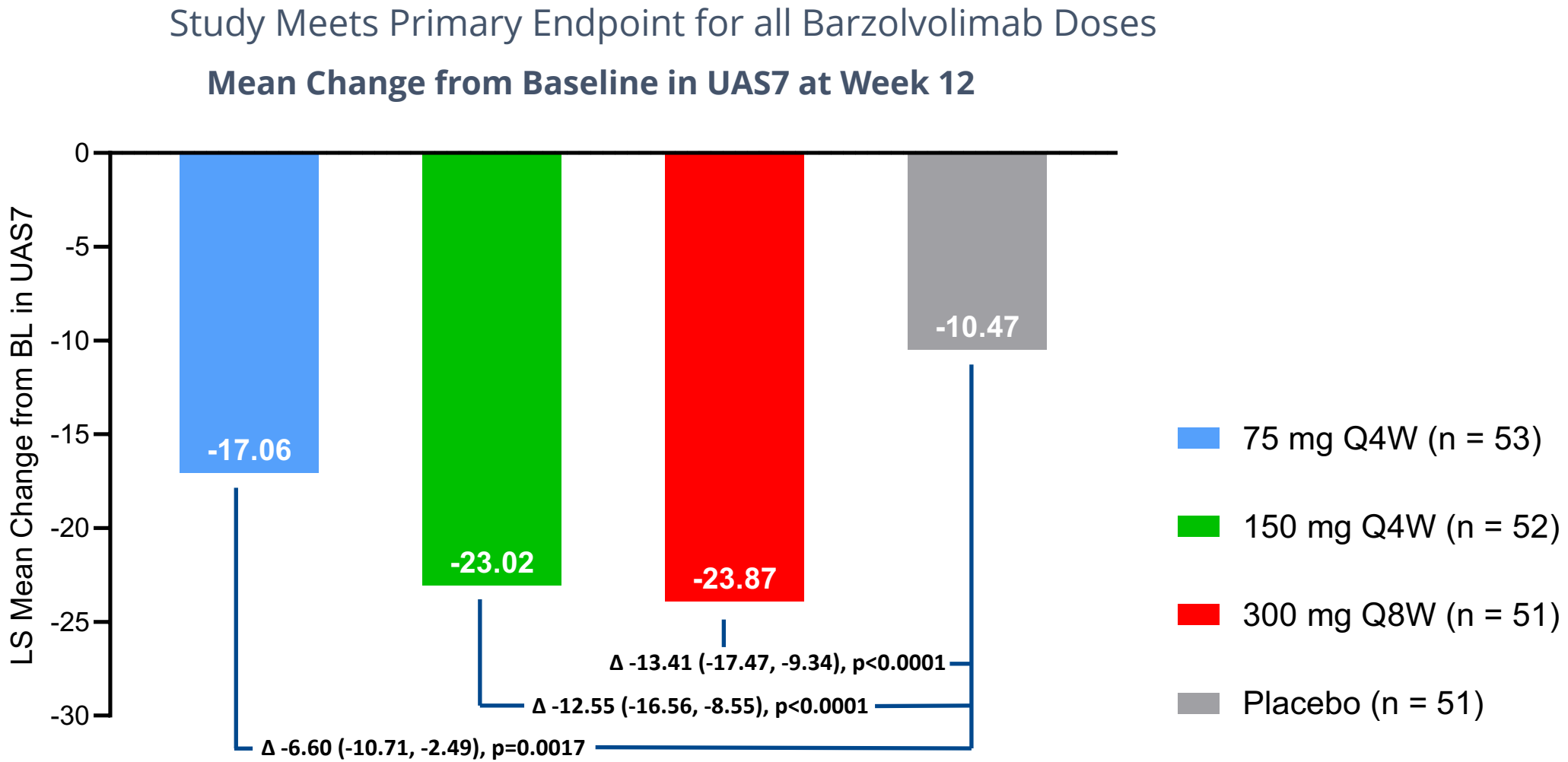
	Barzolvolimab 75 mg Q4W (N= 53)	Barzolvolimab 150 mg Q4W (N= 52)	Barzolvolimab 300 mg Q8W (N= 51)	Placebo (N= 51)
Age (years)	42.2 (15.4)	46.0 (12.8)	47.2 (13.1)	44.4 (15.4)
Gender, Female, n (%)	40 (76%)	39 (75%)	41 (80%)	36 (71%)
Race*				
White, n (%)	40 (76%)	42 (81%)	40 (78%)	40 (78%)
Black, n (%)	9 (17%)	6 (12%)	7 (14%)	7 (14%)
Asian, n (%)	7 (13%)	6 (12%)	4 (8%)	3 (6%)
Weight (kg)	77.5 (20.4)	80.9 (21.4)	85.7 (24.9)	83.8 (19.9)
UAS7 score	30.3 (8.1)	30.8 (7.7)	31.3 (6.9)	30.1 (8.1)
UAS7, severe disease, n (%)	34 (64%)	36 (69%)	39 (76%)	33 (65%)
UCT score	3.74 (2.8)	3.67 (2.5)	2.96 (2.6)	3.38 (2.5)
Angioedema at baseline, n (%)	40 (75%)	35 (67%)	42 (82%)	32 (63%)
Duration of CSU (years)	5.5 (5.4)	5.5 (6.5)	6.3 (6.6)	5.3 (6.6)
Previous experience with omalizumab, n (%)	11 (21%)	11 (21%)	11 (22%)	8 (16%)
Baseline tryptase (ng/ml) (range)	5.9 (<1-36.2)	6.6 (2.8-21.1)	5.7 (<1-15.1)	5.1 (<1-13.9)

Data are mean and standard deviation unless otherwise indicated

*Subjects may be counted in more than one category in the case of multiple races; however, a subject is counted at most once per category

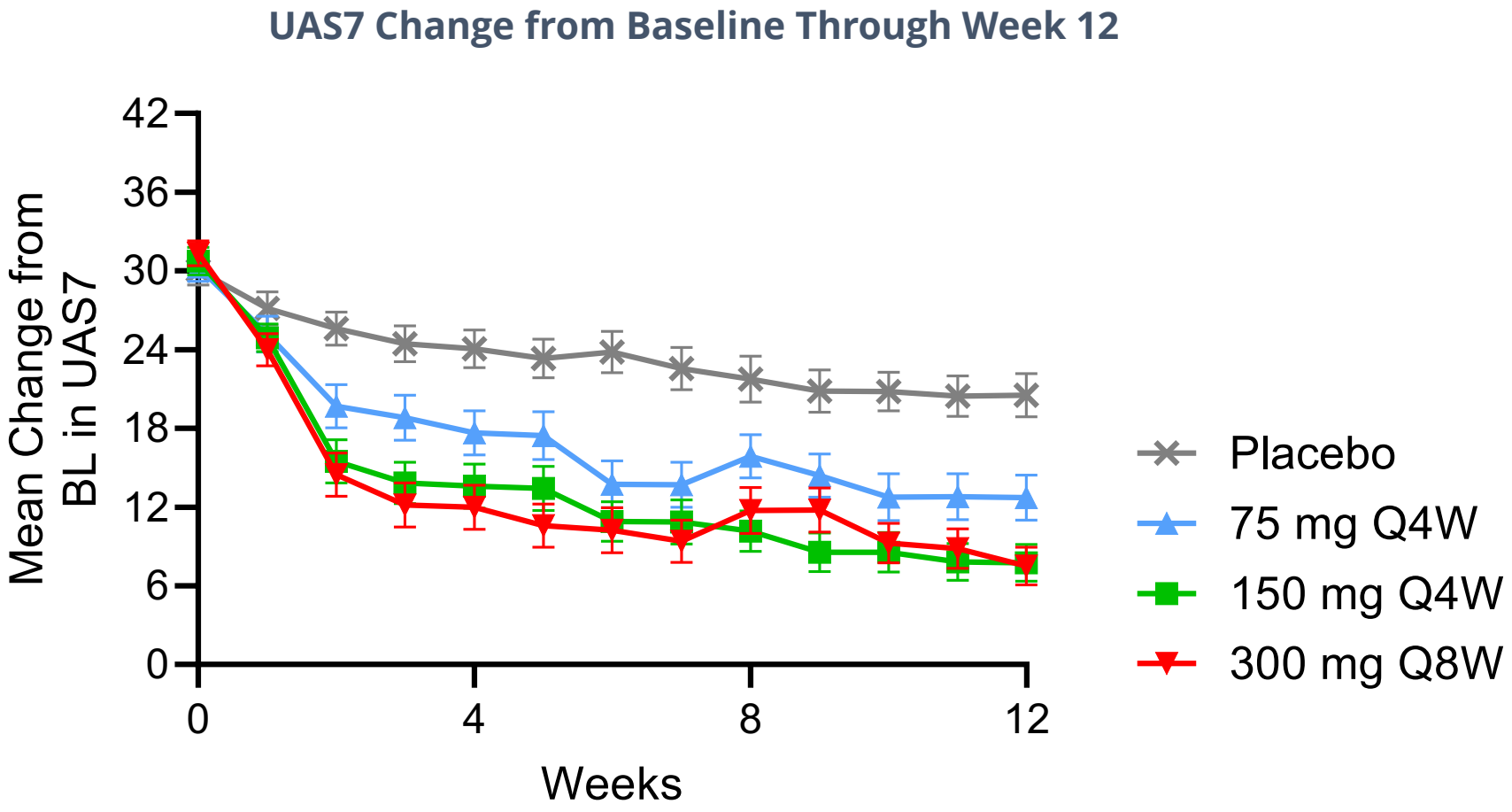
CSU, Chronic Spontaneous Urticaria; UAS7, weekly Urticaria Activity Score; UCT, Urticaria Control Test

Significant Improvement in UAS7 in Patients with Moderate to Severe CSU at all Barzolvolimab Doses



Data were analyzed using ANCOVA model and multiple imputation. Benjamini-Hochberg were used for multiplicity adjustment.
Δ treatment difference LS mean (95% CI)
CI, confidence interval; LS, least squares; n, number of patients who received at least one dose of study drug
UAS7, weekly Urticaria Activity Score

Barzolvolimab Demonstrated Rapid, Significant, and Durable Improvement in UAS7 Score

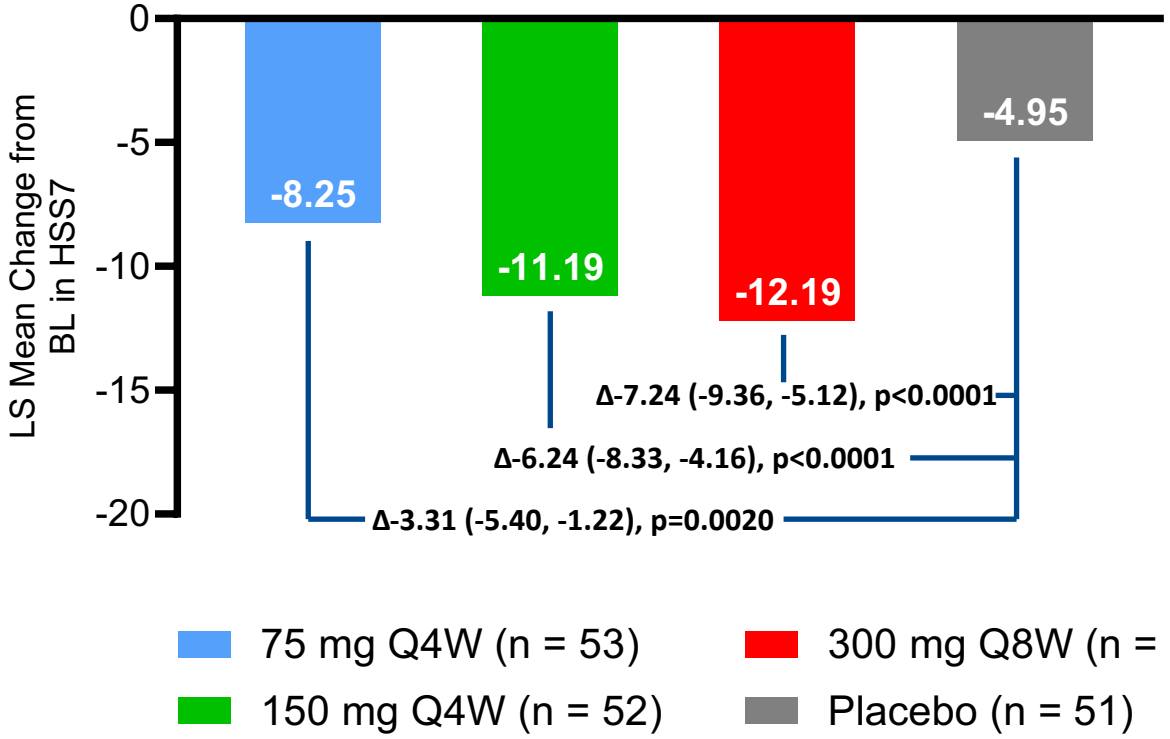


Data are LS mean +/- SE

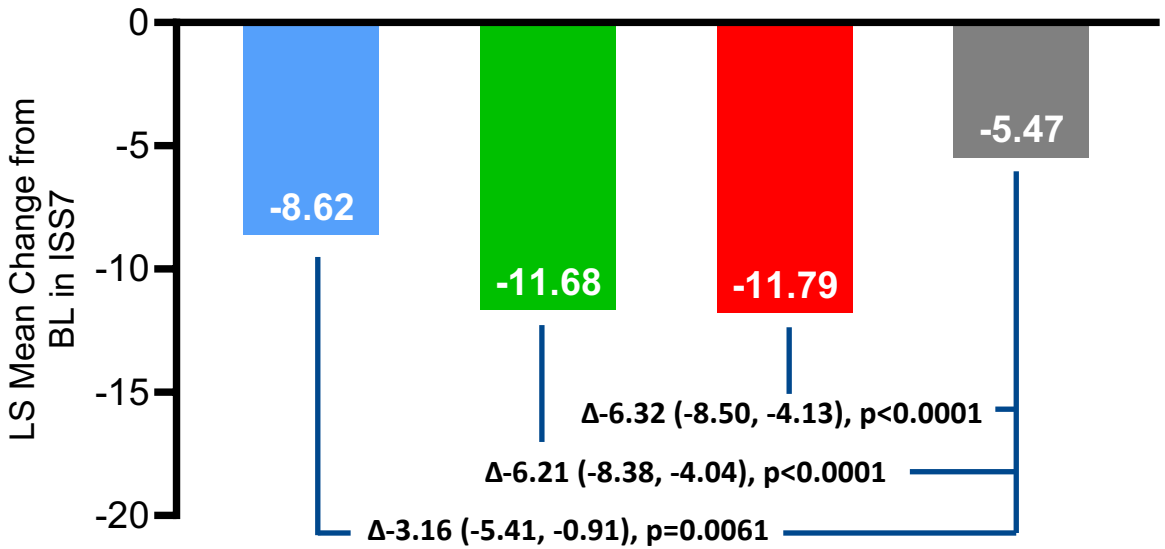
UAS7, weekly Urticaria Severity Score

Statistically Significant and Clinically Meaningful Change From Baseline in HSS7 and ISS7 at Week 12

Mean Change from Baseline in HSS7 at Week 12



Mean Change from Baseline in ISS7 at Week 12



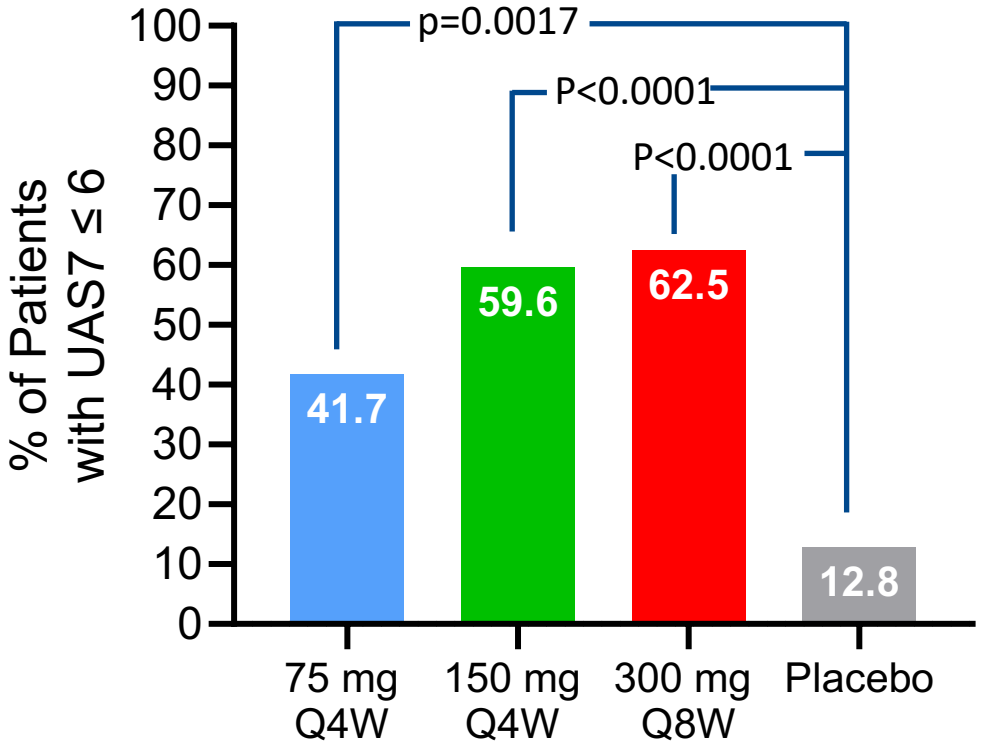
75 mg Q4W (n = 53)
300 mg Q8W (n = 51)
150 mg Q4W (n = 52)
Placebo (n = 51)

Data were analyzed using ANCOVA model and multiple imputation
Δ treatment difference LS mean (95% CI)
CI, confidence interval; LS, least squares; n, number of patients who received at least one dose of study drug
HSS7, weekly Hives Severity Score; ISS7, weekly Itch Severity Score

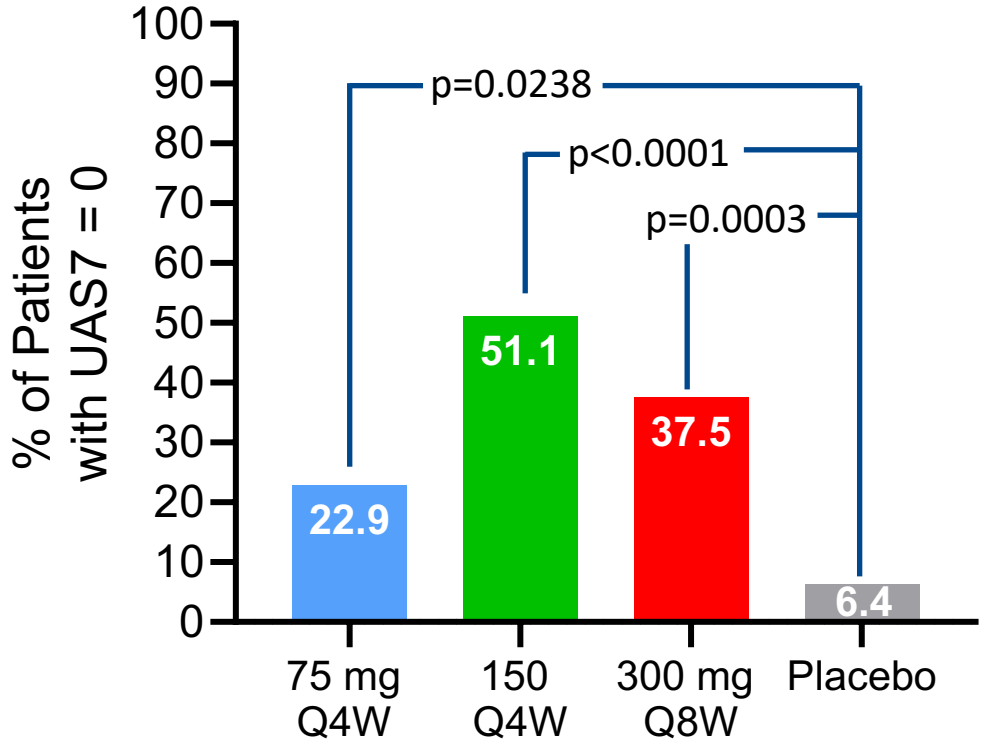
Enhanced Disease Control with Barzolvolimab at Week 12

Significantly more patients treated with barzolvolimab compared to placebo had well controlled disease (UAS7≤ 6) or achieved a complete response (UAS7=0)

% of Patients with UAS7≤ 6 Well Controlled

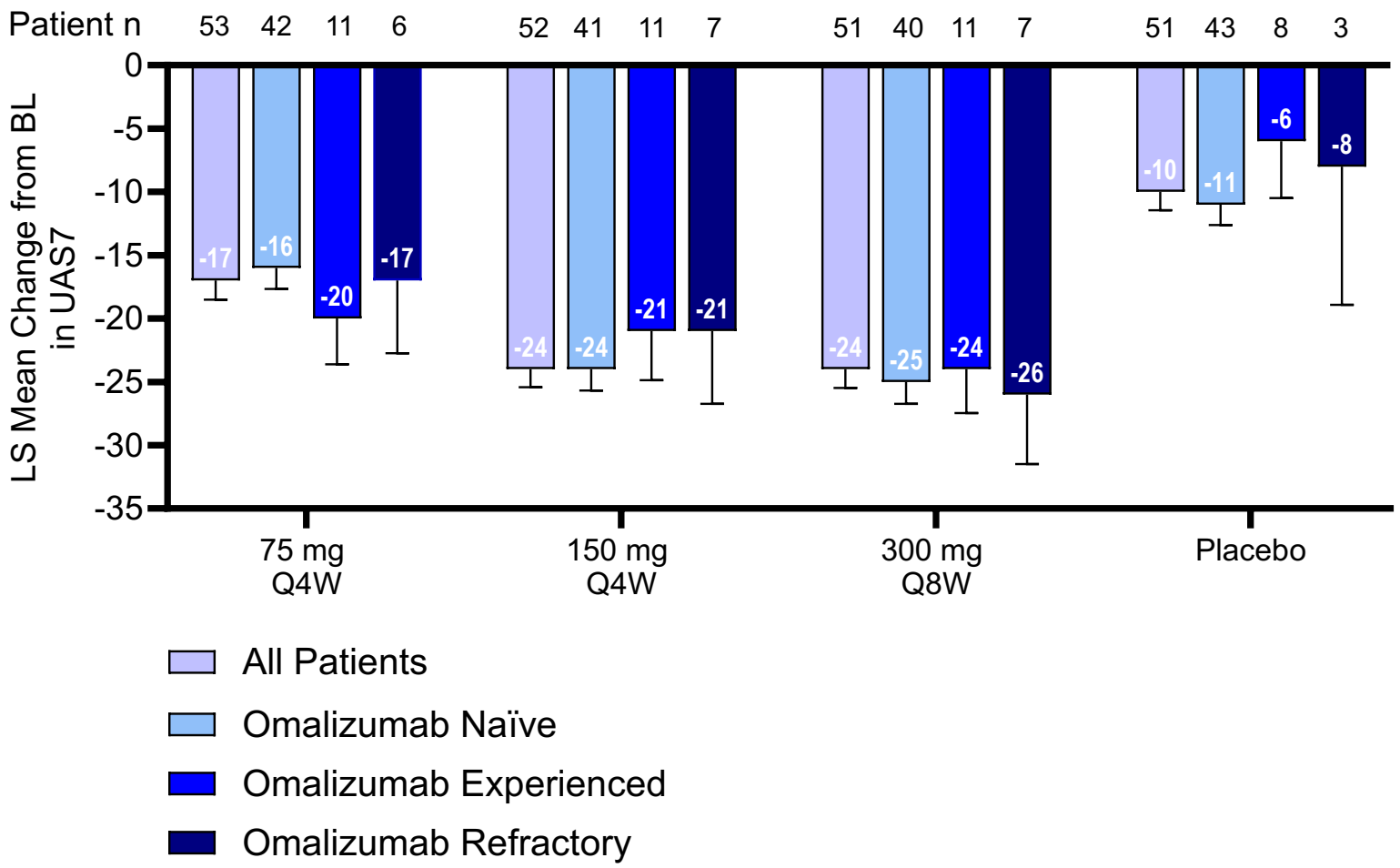


% of Patients with UAS7=0 Complete Control



Data were analyzed under mITT population with Cochran-Mantel-Haenszel tests for comparison between each active dosing regimen versus placebo.
UAS7, weekly Urticaria Activity Score

Comparable Improvement in UAS7 in Omalizumab Naïve and Experienced/Refractory* Patients at Week 12



Data are LS mean +/- SE

*Omalizumab refractory is a subset of omalizumab experienced patients who have had an inadequate clinical response or were intolerant to omalizumab

Barzolvolimab Demonstrated a Favorable Safety Profile at all Doses

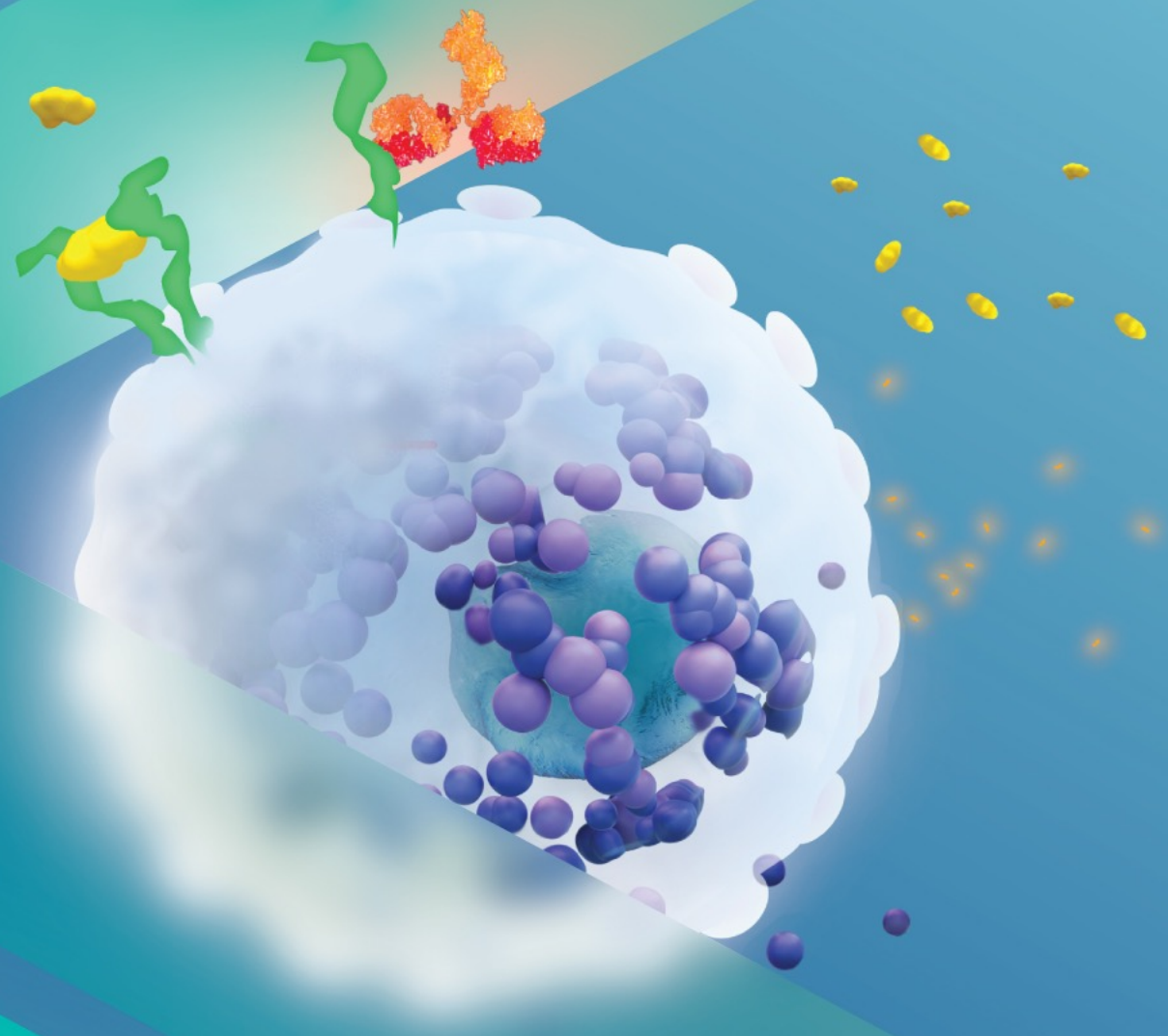
Patients, n (%)	Barzolvolimab 75 mg Q4W (N= 53)	Barzolvolimab 150 mg Q4W (N= 52)	Barzolvolimab 300 mg Q8W (N= 51)	Any barzolvolimab dose (N= 156)	Placebo (N= 51)
Patients with ≥1 AE	28 (53)	29 (56)	31 (61)	88 (56)	14 (28)
Patients with SAE(s)	0	0	1 (2)	1 (1)	0
Discontinued study treatment due to AE(s)	2 (4)	1 (2)	4 (8)	7 (4)	0
Most frequent AEs by primary system organ class (≥10% of all patients receiving any barzolvolimab dose)					
Skin and subcutaneous tissue disorders	10 (19)	11 (21)	14 (28)	35 (22)	5 (10)
Infections and Infestations	9 (17)	9 (17)	12 (24)	30 (19)	9 (18)
Nervous System Disorders	5 (9)	6 (12)	7 (14)	18 (12)	0
Most frequent AEs by Preferred Term (≥10% of patients in any treatment group)					
Urticaria/CSU	8 (15)	5 (10)	3 (6)	16 (10)	5 (10)
Hair color changes	0	5 (10)	9 (18)	14 (9)	0
Neutropenia	4 (8)	3 (6)	5 (10)	12 (8)	0

Most AEs were mild to moderate in severity; infections were not accompanied by neutropenia
SAE of external ear canal cholesteatoma considered unrelated to treatment
Discontinuations due to AE: neutropenia, abdominal pain, hair color change, hair color change/dizziness, urticaria, neutropenia/thrombocytopenia

Conclusions

- In this ongoing Phase 2 study, barzolvolimab, an anti-KIT mAb, demonstrated a statistically significant and clinically meaningful decrease in UAS7 vs placebo at Week 12 in patients with CSU who are symptomatic on antihistamines
  - The majority of patients had well controlled urticaria at Week 12 (UAS7≤6)
  - UAS7=0 was observed in 51% of patients in the 150 mg Q4W and in 37.5% of patients in the 300 mg Q8W groups compared to 6.4% in the placebo group
  - Sustained activity with rapid onset within 2 weeks
  - Statistically significant and clinically meaningful decrease in both ISS7 and HSS7 at Week 12
  - Similar pattern of improvement observed in patients with omalizumab-experienced/refractory and omalizumab-naïve CSU consistent with mechanism of action
- Barzolvolimab demonstrated a favorable safety profile across the dose ranges studied
- Phase 3 studies are planned to initiate in 2024

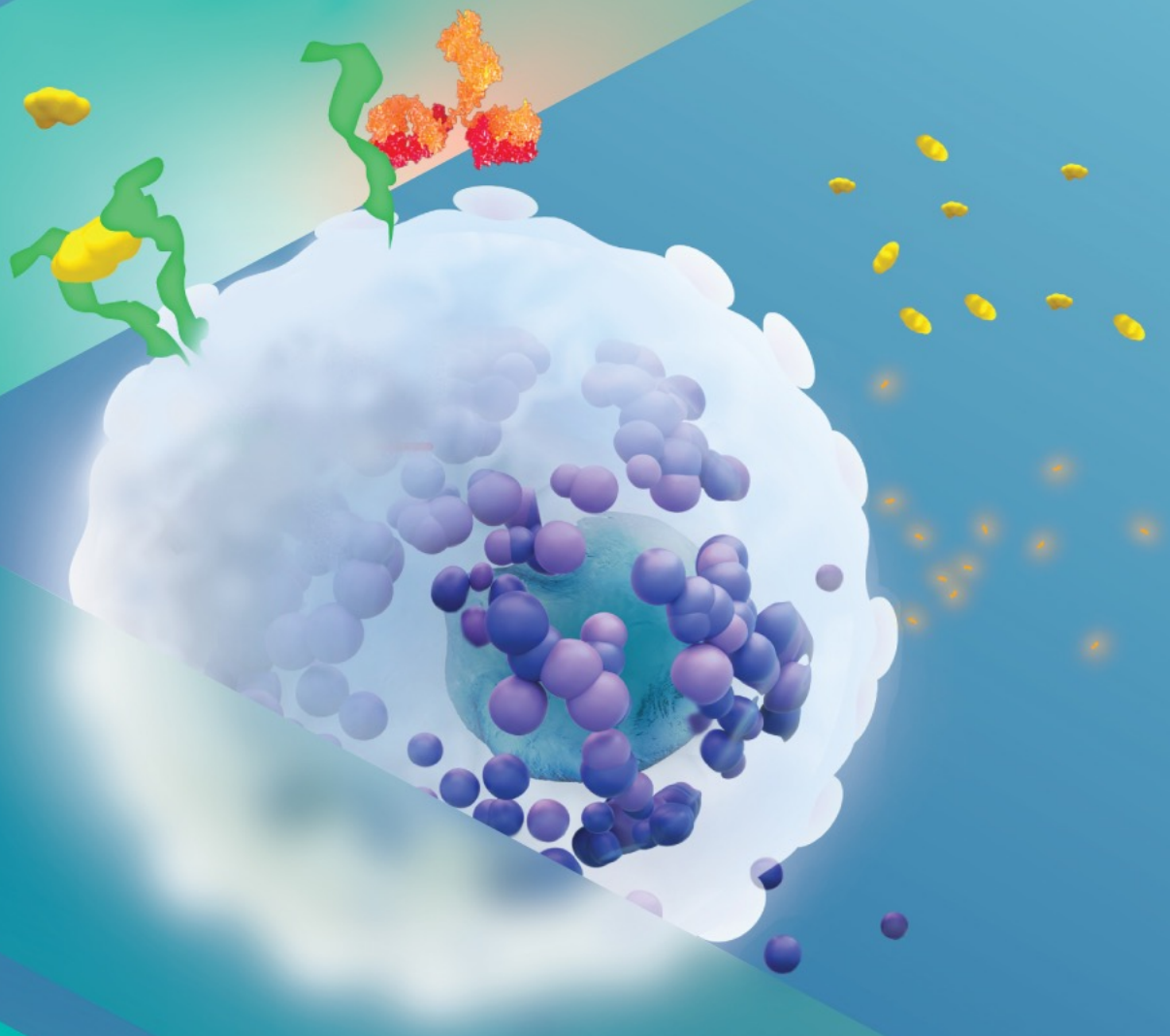
Celldex therapeutics



Discussion/Comments

Allan Kaplan, MD
Professor of Medicine, Division of Pulmonary, Critical Care, Allergy and Immunology at the Medical University of South Carolina

Celldex therapeutics



Questions